Analysis of cytolyic immunity models

Contents

Overview

This document goes over the analysis of the model results from the main model described in the manuscript: CMV infection with cytolytic immune response (see model_code_documentation/CMV_Models.pdf for equations and code). The immune parameters for this model are fit across the entire episode for each infant. The beta and start_time parameters were fit to the expansion phase only in a prior analysis to estimate R0 (see first results section of target_cell_model_analysis.pdf for that).

This document and code generated the results presented for publication: Figures 3 and 4 come from here. This is how the analysis was broken down:

1. Assessement of optimized parameter values and model fit
2. Model results interpretation through simulation using best fits and estimation of infected cell lifespan with immune response
3. Estimation of effective reproduction number, R, to evaluate critical time points during infection
4. Check on epithelial cell loss

Model optimization and results

Model parameters were estimated for each infant episode after initializing. Subject by subject parameters and model fits appear in the results_figures/

Fitted model parameters

	PatientID2	theta	log10KI	gammaX100	mse
1	A	1.34	0.87	2.24	38.30
2	B	0.23	2.87	0.73	31.76
3	C	0.42	1.92	0.78	28.53
4	D	20.97	8.00	0.08	26.54
5	E	0.98	2.84	1.38	10.78
6	F	2.78	0.80	2.68	17.45
7	G	1.42	3.23	2.57	16.15
8	H	100.00	5.77	0.23	21.13
9	I	0.68	1.52	0.98	12.73
10	J	1.38	1.82	1.65	17.56
11	K	0.96	2.13	1.51	20.96
12	L	1.63	2.03	1.61	14.21
13	M	6.72	1.75	3.59	9.39
14	N	1.72	2.91	3.67	6.74

Table 1: Supplementary Table - Fits from cytolytic immune model

Simulated data fit compared to episode data (Figure 3)

(also saves figure results_figures/CTL_model_fits.pdf that displays parameter values, R0 along with time series plots. This chunk has eval = F in the code.)

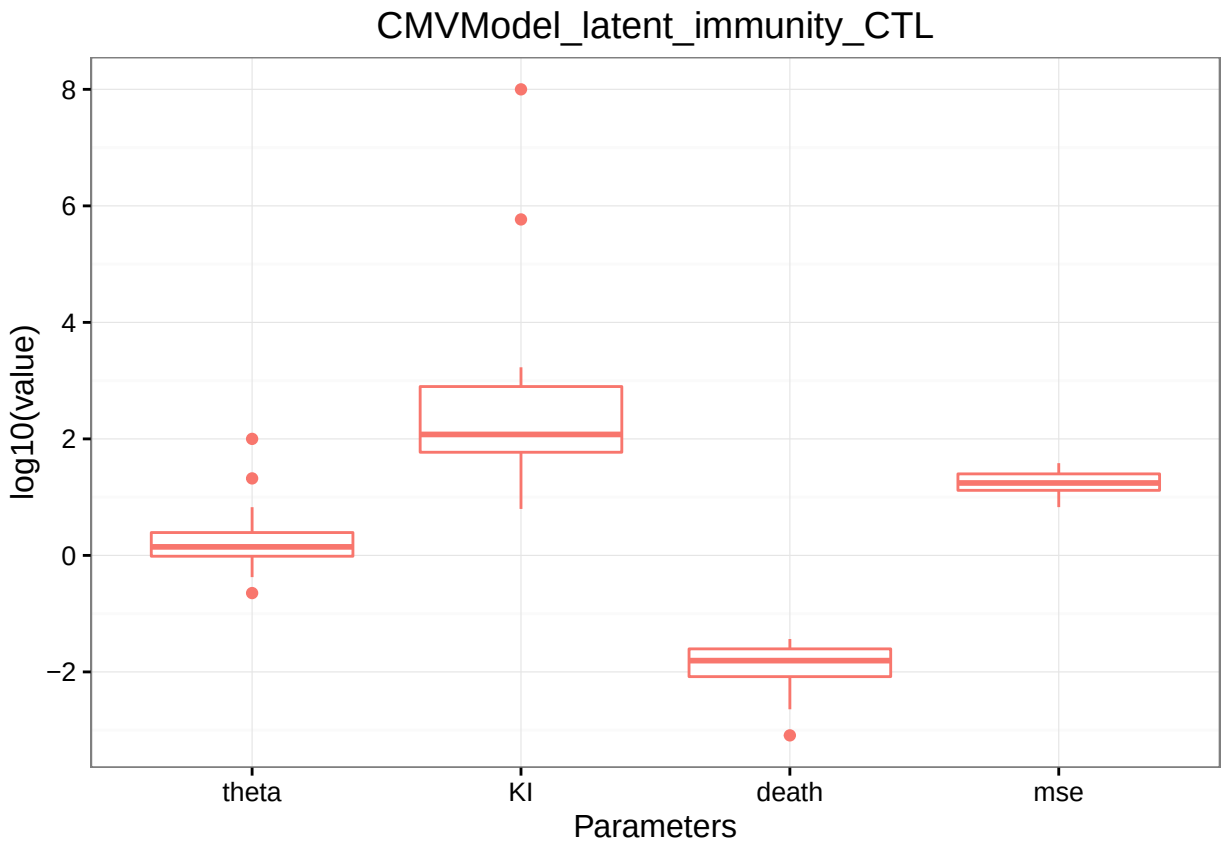


Figure 1: Parameter boxplots

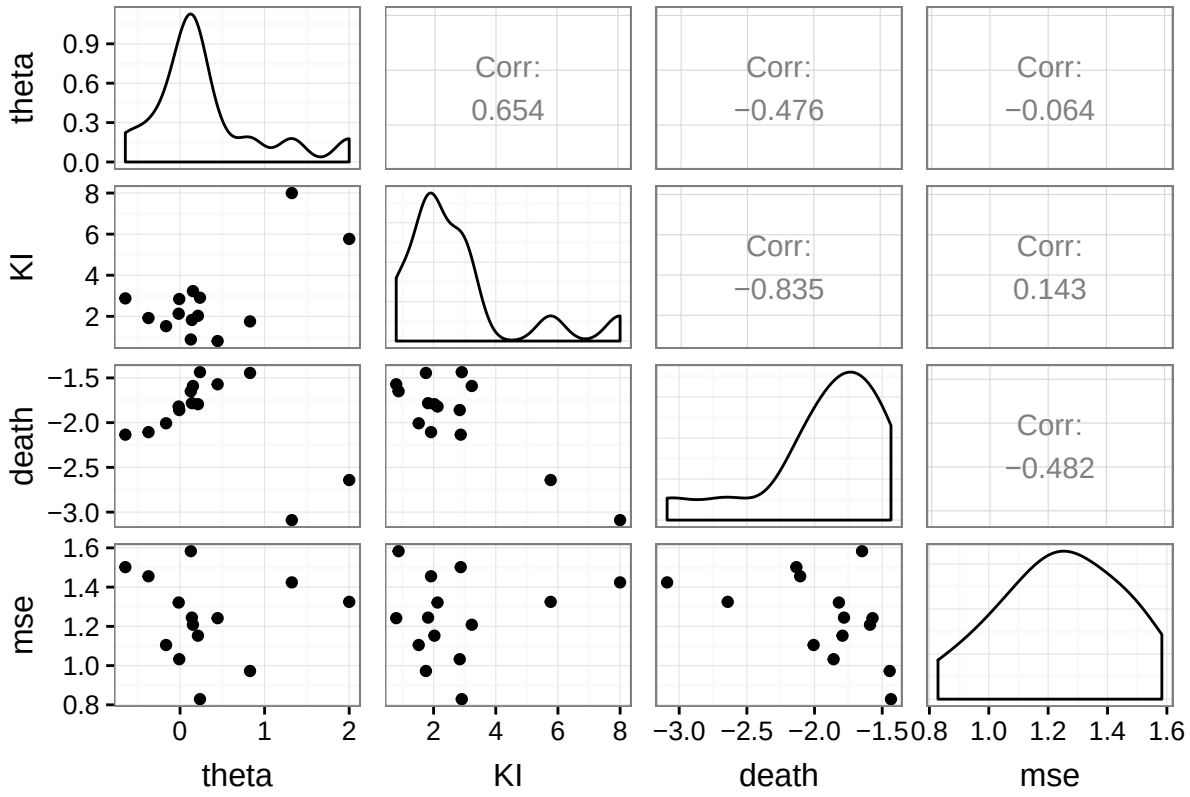
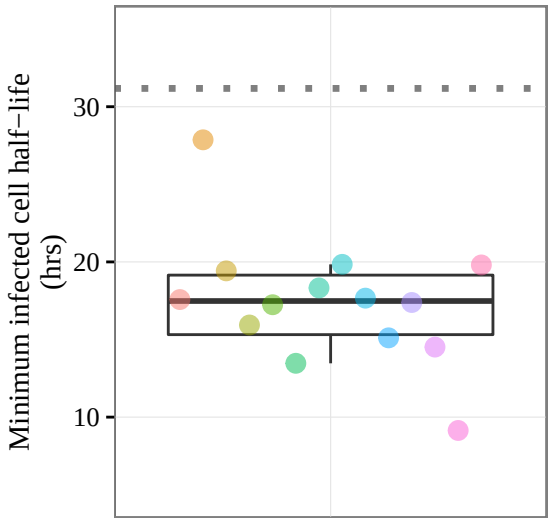


Figure 2: Distribution and correlation of fitted immune parameters (all transformed log10)

Infected cell lifespan with immune pressure

Time series plots of immune pressure

Magnitude of peak response (shortest infected cell lifespan)



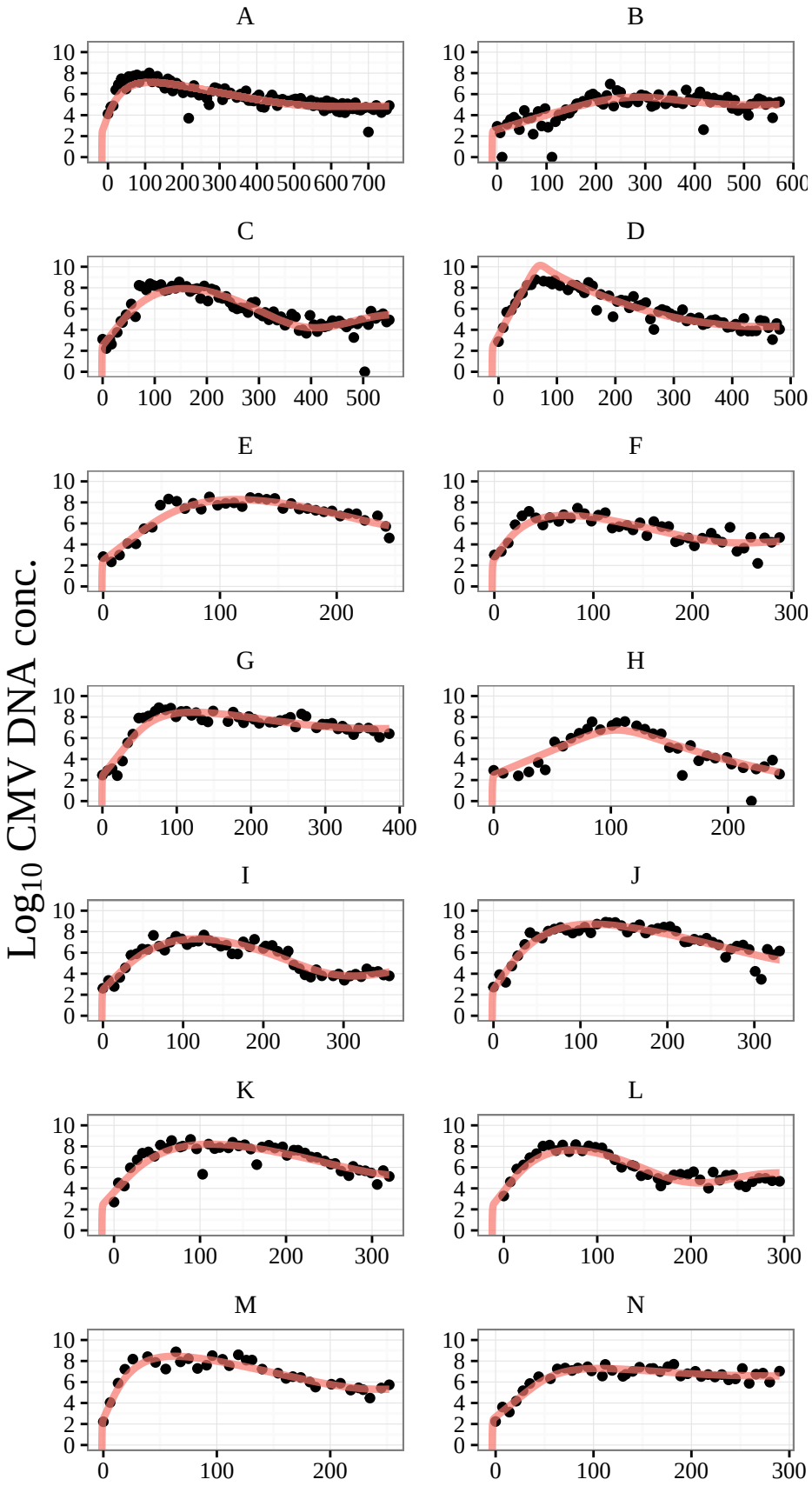


Figure 3: Best immune model fits

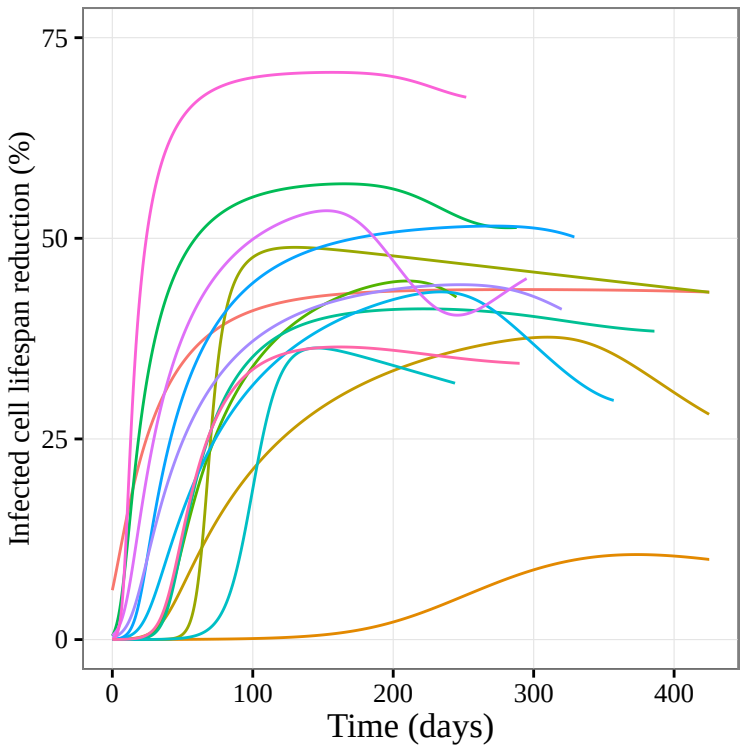


Figure 4: Immune pressure over time on infected cell lifespan

Time of peak response (when shortest infected cell lifespan)

Effective reproduction number

Clearance phase initiation and effective R == 1

When effective R crosses 1 for the first time, that initiates clearance. This matches with the peak viral load day predicted in the model as expected (with some round error)

Comparing clearance phase initiation and peak immune response day

Clearance phase initiation equivalent to first day that R = 1. It happens much earlier than the peak immune pressure day.

Minimum effective R vs R0

Effective R over time

Immune effect on epithelial cell population

Only one of the model predicts substantial population depletion

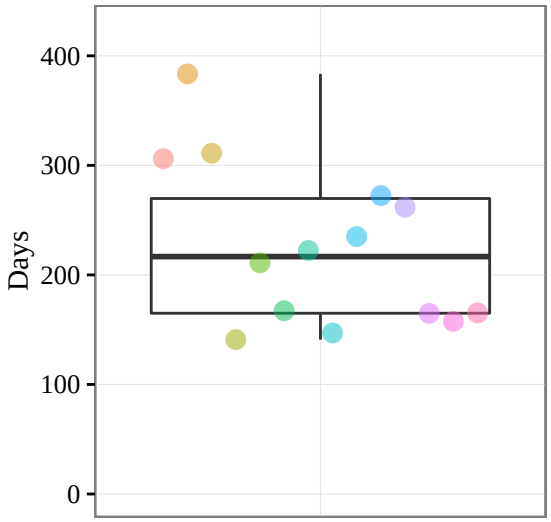


Figure 5: distribution of peak immune pressure

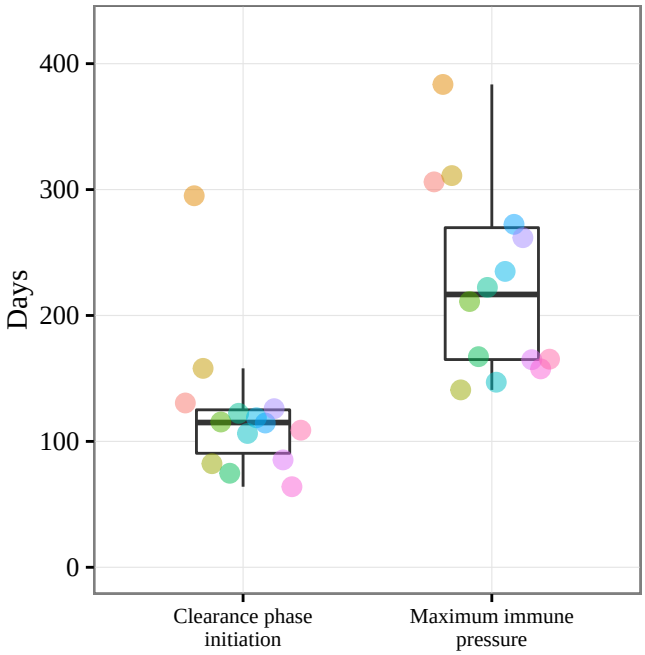


Figure 6: distribution of days for critical immune times

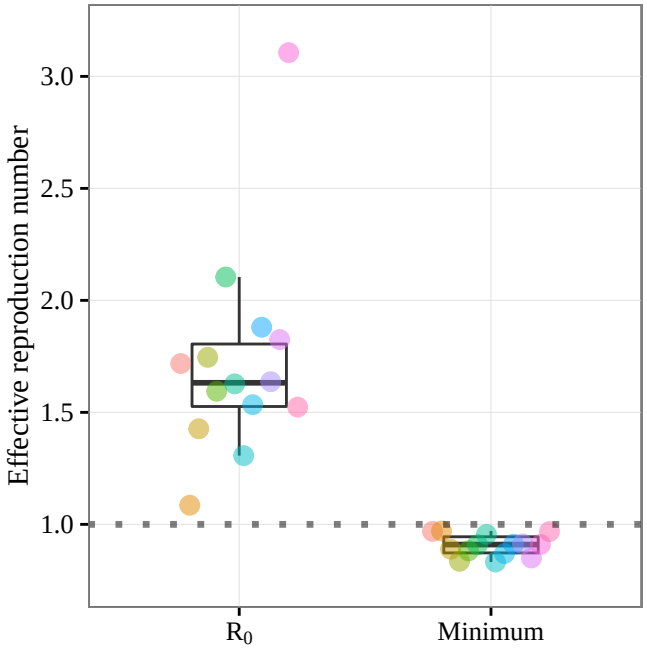


Figure 7: R0 vs minimum R

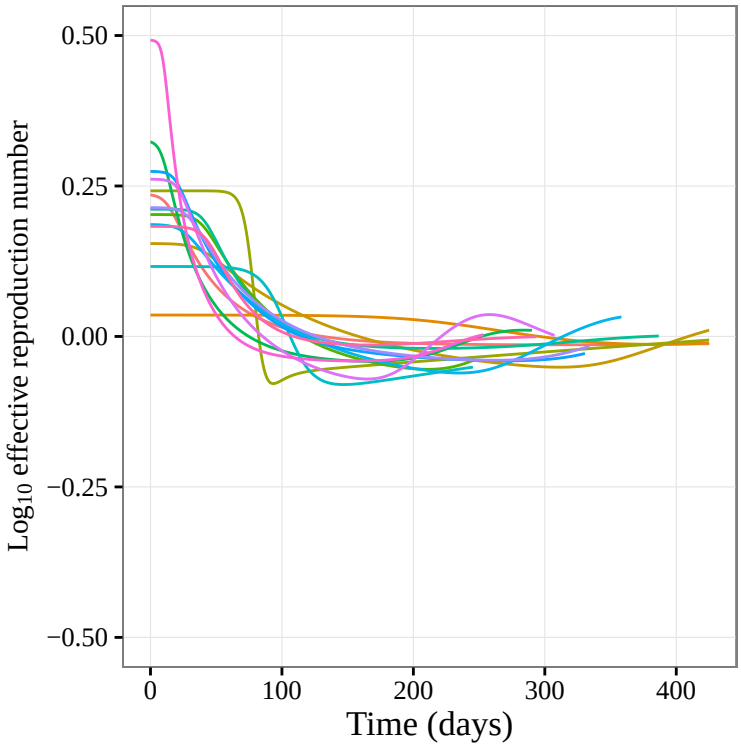


Figure 8: Immune pressure over time on infected cell lifespan

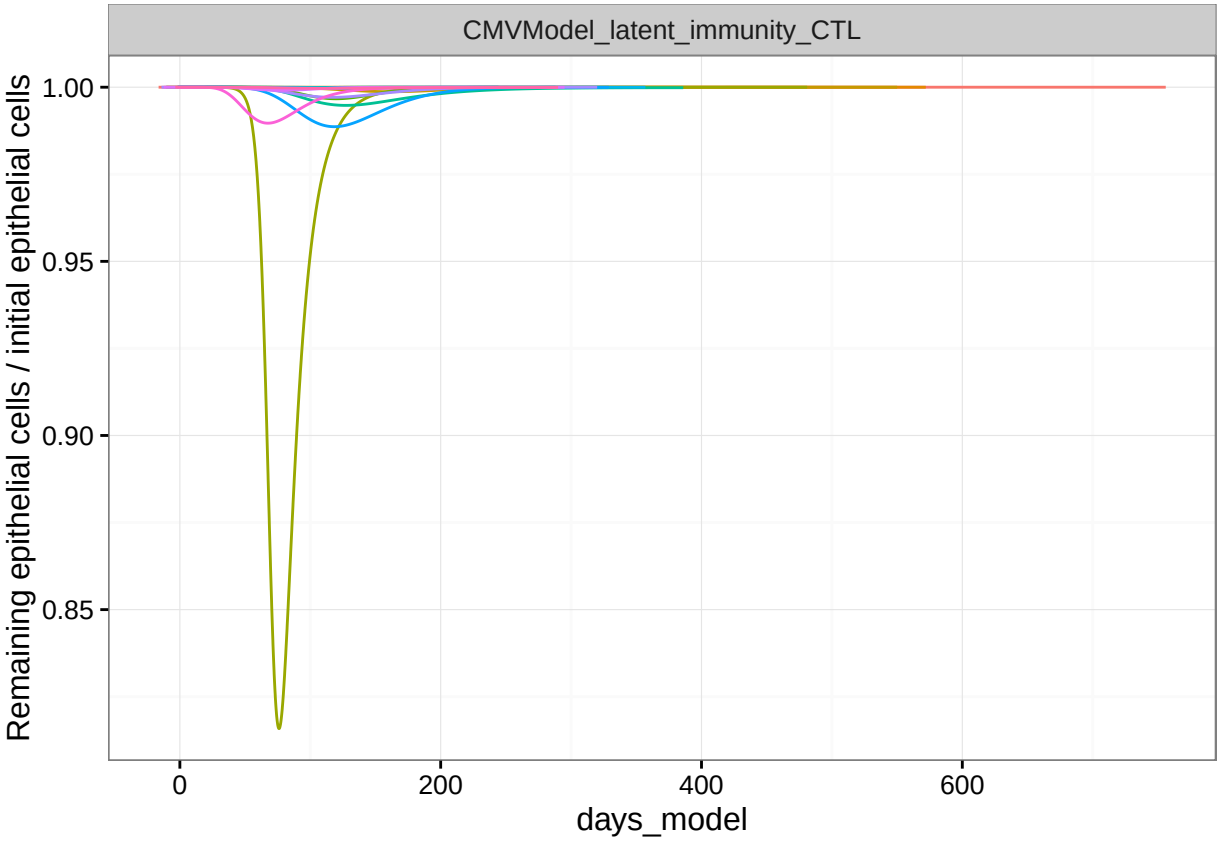


Figure 9: Population depletion of epithelial cells

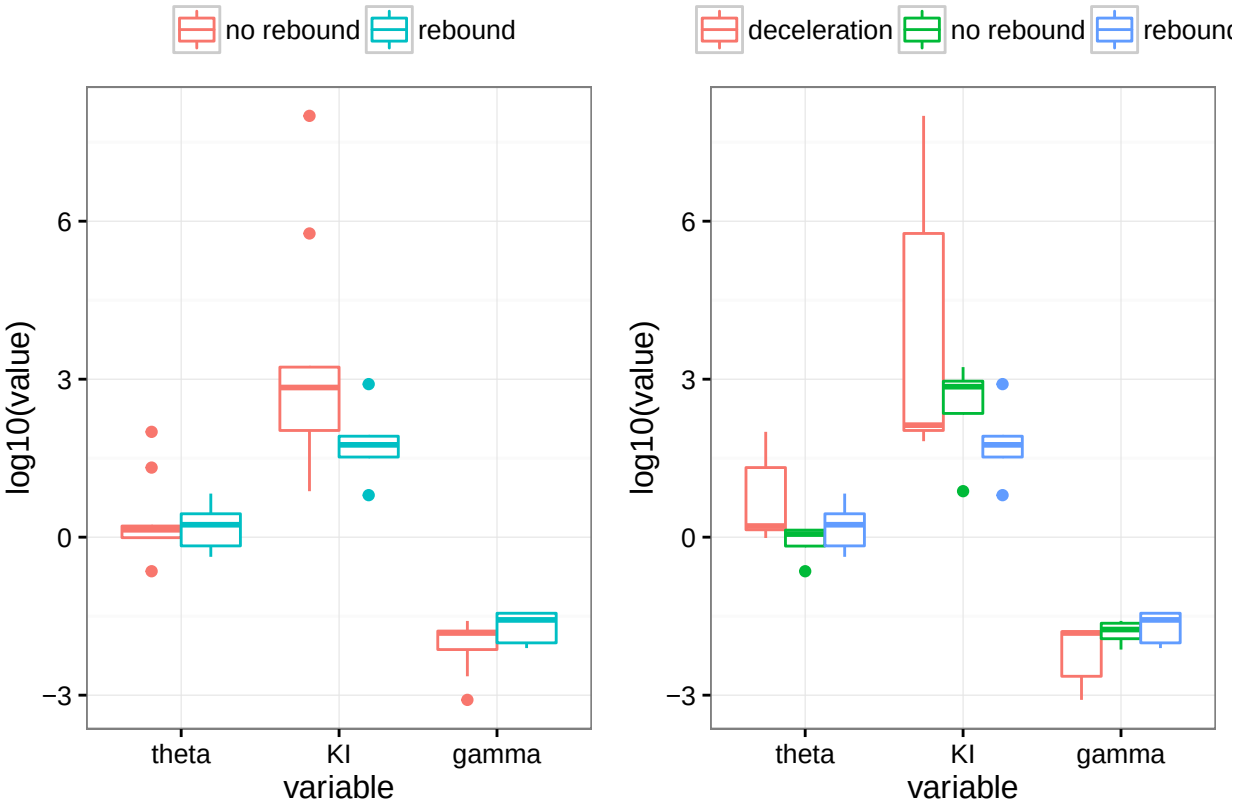
PatientID2	minimum_lifespan_hrs	maximum_reduction_pct
A	17.57	43.61
B	27.87	10.59
C	19.42	37.68
D	15.93	48.88
E	17.24	44.68
F	13.47	56.79
G	18.32	41.21
H	19.84	36.34
I	17.66	43.33
J	15.11	51.53
K	17.39	44.22
L	14.51	53.44
M	9.14	70.68
N	19.80	36.46

Table 2: Maximum immune pressure effect on infected cell lifespan (compared to 31 hours without immunity)

variable	median	IQR	range
minimum_lifespan_hrs	17.48	15.314, 19.149	9.139, 27.867
maximum_reduction_pct	43.92	38.564, 50.866	10.593, 70.68

Table 3: Summary of maximum immune pressure effect on infected cell lifespan (compared to 31 hours without immunity)

Rebound parameters



PatientID2	peak_immune_day
A	306.10
B	383.50
C	311.10
D	140.90
E	211.10
F	167.30
G	222.30
H	147.00
I	235.00
J	272.40
K	261.80
L	164.90
M	157.60
N	165.30

Table 4: Day of peak immune pressure

median	IQR	range
216.70	165, 269.75	140.9, 383.5

Table 5: Summary stats for day of immune pressure

Save output data and figures.

See code for this.

PatientID2	peak_viral_day	effectiveR_eq1_day
A	130.90	130.50
B	295.80	295.10
C	158.20	158.00
D	82.50	82.30
E	115.40	115.40
F	74.60	74.70
G	122.40	122.30
H	106.30	106.30
I	118.80	118.80
J	114.70	114.60
K	126.10	126.00
L	85.20	85.30
M	63.80	64.00
N	109.10	108.90

Table 6: Day of peak viral load (clearance start) and when R = 1

variable	median	IQR	range
peak_viral_day	115.05	90.475, 125.175	63.8, 295.8
effectiveR_eq1_day	115.00	90.55, 125.075	64, 295.1

Table 7: Summary stats for day of peak viral load (clearance start) and when R = 1

PatientID2	R0	minR
A	1.72	0.97
B	1.09	0.97
C	1.43	0.89
D	1.75	0.84
E	1.59	0.88
F	2.10	0.91
G	1.63	0.96
H	1.31	0.83
I	1.53	0.87
J	1.88	0.91
K	1.64	0.91
L	1.82	0.85
M	3.11	0.91
N	1.52	0.97

Table 8: R0 and minimum effective R

variable	median	IQR	range
R0	1.632	1.526, 1.805	1.085, 3.106
minR	0.910	0.873, 0.945	0.832, 0.97

Table 9: Summary stats for R0 and minimum effective R

PatientID2	max_loss
A	0.000
B	0.000
C	0.001
D	0.146
E	0.003
F	0.000
G	0.004
H	0.000
I	0.000
J	0.009
K	0.002
L	0.001
M	0.008
N	0.000

Table 10: Maximum cell loss (percent)

median_pct_loss	range_pct_loss
0.001	0, 0.146

Table 11: Summary of maximum cell loss (percent)

rebound_cat	median theta	median log10 KI)	median effector lifespan (1/gamma)
no rebound	1.38	2.84	66.05
rebound	1.72	1.75	37.27

Table 12: Immune parameter differences by rebound status (two category)

rebound_cat2	median theta	median log10 KI)	median effector lifespan (1/gamma)
deceleration	1.63	2.13	66.05
no rebound	1.16	2.86	55.14
rebound	1.72	1.75	37.27

Table 13: Immune parameter differences by rebound status